

Remarks

Applicants have attached an abstract on a separate sheet of paper as required by U.S. practice. Applicants have amended the specification for purposes of adding the priority information. Claims 1-17, 19, 20 and 24-29 remain in this application. Claims 18 and 21-23 have been cancelled. Claims 3, 4, 5, 14, 15, 19, 20, 24, 26 and 29 have been amended to remove multiple dependency. A copy of the claims are attached for the Examiner's convenience. It is respectfully submitted that the present application is in condition for allowance. An early consideration and notice of allowance are earnestly solicited.

Respectfully submitted,

Date: 22 October 2001

Robert H. Brink

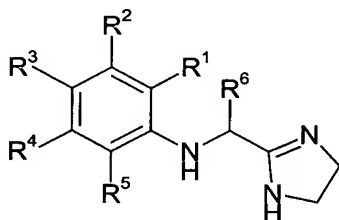
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Version With Markings To Show Changes Made

1. A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof,

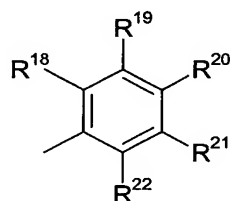


(I)

wherein  $R^2$ ,  $R^3$ ,  $R^4$ , and  $R^5$  are independently H, halogen, -OH, -C<sub>1-3</sub>alkyl, -C<sub>1-3</sub>alkoxy, -SC<sub>1-2</sub>alkyl, or -CF<sub>3</sub>, with the proviso that at least 2 of  $R^2$ ,  $R^3$ ,  $R^4$ , and  $R^5$  are H;

$R^6$  is H or -CH<sub>3</sub>;

$R^1$  is -S(O)<sub>n</sub>R<sup>7</sup> where n is 1 or 2, -S(O)<sub>2</sub>NHR<sup>8</sup>, -C(O)R<sup>9</sup>, -NR<sup>14</sup>R<sup>15</sup>, -C(R<sup>17</sup>)=NOR<sup>16</sup>,

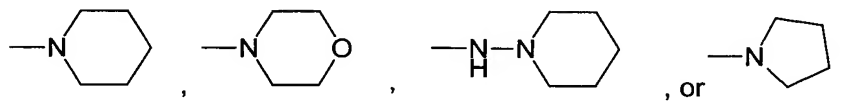


or a 5, 6, or 7 membered heteroalkyl or heteroaryl group optionally substituted with 1 or two groups selected from the group consisting of the following substituents for carbon: C<sub>1-3</sub>alkyl, -CH<sub>2</sub>CF<sub>3</sub>, -CF<sub>3</sub>, F, Cl, C<sub>1-2</sub>alkoxy, C<sub>1-2</sub>thioalkyl, and the following substituents for nitrogen: C<sub>1-3</sub>alkyl and -CH<sub>2</sub>C<sub>1-2</sub>fluoroalkyl;

$R^7$  is C<sub>1-3</sub>alkyl or C<sub>1-2</sub>fluoroalkyl;

$R^8$  is C<sub>1-3</sub>alkyl or -CH<sub>2</sub>C<sub>1-2</sub>fluoroalkyl;

$R^9$  is C<sub>1-3</sub>alkyl optionally substituted with 1-3 fluorine atoms, -NR<sup>10</sup>R<sup>11</sup>, -NHNH<sup>12</sup>R<sup>13</sup>, -CH<sub>2</sub>SO<sub>2</sub>CH<sub>3</sub>,



R<sup>10</sup> is H or C<sub>1</sub>-2alkyl;

R<sup>11</sup> is H, cyclopropyl, cyclopropylmethyl, C<sub>3</sub>-6alkenyl with the proviso that any unsaturation is not adjacent to the depicted nitrogen, or C<sub>1</sub>-6alkyl optionally substituted with hydroxy, C<sub>1</sub>-3alkoxy, or 1-3 fluorine atoms with the proviso that the carbon atom in R<sup>11</sup> that is bonded to the depicted nitrogen is not bonded to either a fluorine or an oxygen;

R<sup>12</sup> is H or C<sub>1</sub>-2alkyl;

R<sup>13</sup> is H, C<sub>3</sub>-5cycloalkyl, cyclopropylmethyl, -SO<sub>2</sub>CH<sub>3</sub>, -C(O)CH<sub>3</sub>, C<sub>3</sub>-6alkenyl with the proviso that any unsaturation is not adjacent to the depicted nitrogen, or C<sub>1</sub>-6alkyl optionally substituted with hydroxy, C<sub>1</sub>-3alkoxy, or 1-3 fluorine atoms with the proviso that the carbon atom in R<sup>13</sup> that is bonded to the depicted nitrogen is not bonded to either a fluorine or an oxygen,;

R<sup>14</sup> is H or C<sub>1</sub>-2alkyl;

R<sup>15</sup> is C<sub>3</sub>-5cycloalkyl, cyclopropylmethyl, C<sub>3</sub>-6alkenyl with the proviso that any unsaturation is not adjacent to the depicted nitrogen, or C<sub>1</sub>-6alkyl optionally substituted with hydroxy, C<sub>1</sub>-3alkoxy, or 1-3 fluorine atoms with the proviso that the carbon atom in R<sup>15</sup> that is bonded to the depicted nitrogen is not bonded to either a fluorine or an oxygen;

R<sup>16</sup> is C<sub>1</sub>-2alkyl;

R<sup>17</sup> is H or C<sub>1</sub>-3alkyl;

R<sup>20</sup> is H; and

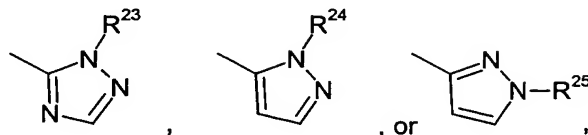
R<sup>18</sup>, R<sup>19</sup>, R<sup>21</sup>, and R<sup>22</sup> are independently H, halogen, hydroxy, C<sub>1</sub>-3alkyl, C<sub>1</sub>-3alkoxy, -SC<sub>1</sub>-2alkyl, or -CF<sub>3</sub> with the proviso that at least one of R<sup>18</sup>, R<sup>19</sup>, R<sup>21</sup>, or R<sup>22</sup> is other than H.

2. A compound of Claim 1 wherein R<sup>2</sup>, R<sup>3</sup>, and R<sup>5</sup> are H or F.

3. (AMENDED) A compound of [Claim 1 or] Claim 2 wherein R<sup>4</sup> = H, F, Cl, -OCH<sub>3</sub>, or -CH<sub>3</sub>.

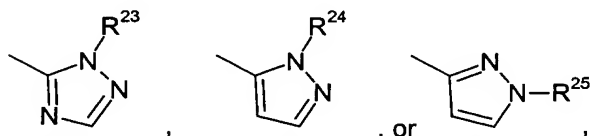
4. (AMENDED) A compound of [any of] Claim [1] 3 wherein R<sup>6</sup> is H.

5. (AMENDED) A compound of [any of] Claim [1] 4 wherein  $R^1$  is -  
 $S(O)_nR^7$ ,  $S(O)_2NHR^8$ ,



where  $R^{23}$  is H, C<sub>1</sub>-alkyl, or 2,2,2-trifluoroethyl,  $R^{24}$  is H, C<sub>1</sub>-alkyl, or 2,2,2-trifluoroethyl, and  $R^{25}$  is H, methyl, or ethyl.

6. A compound of Claim 5 where  $R^1$  is



where  $R^{23}$  is isopropyl or 2,2,2-trifluoroethyl,  $R^{24}$  is methyl or ethyl, and  $R^{25}$  is methyl, or ethyl.

7. A compound of Claim 5 wherein  $R^1$   $S(O)_2NHR^8$ .

8. A compound of Claim 7 wherein  $R^8$  is CH<sub>3</sub>.

9. A compound of Claim 5 wherein  $R^1$  is  $-S(O)_nR^7$ .

10. A compound of Claim 9 wherein n is 2 and  $R^7$  is CH<sub>3</sub>.

11. A compound of Claim 1 selected from the group consisting of  
 2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-propylbenzamide,  
 N-cyclopropyl-2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]benzamide,  
 2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-methylbenzamide,  
 {2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]phenyl}(4-morpholinyl)methanone,  
 2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N,N-diethylbenzamide,  
 2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-ethyl-N-methylbenzamide,  
 2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-methyl-N-propylbenzamide,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1,3-oxazol-5-yl)aniline,

1-{2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]phenyl}-1-ethanone,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(2-pyrazinyl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(2-methyl-1,3-thiazol-4-yl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-methyl-1H-pyrazol-3-yl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-methyl-1H-pyrazol-5-yl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(methylsulfonyl)aniline,  
 2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-methylbenzenesulfonamide,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-methyl-1H-pyrrol-2-yl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-ethyl-1H-pyrazol-3-yl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-ethyl-1H-pyrazol-5-yl)aniline,  
 2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-ethylbenzenesulfonamide,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-ethyl-1H-pyrrol-2-yl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-[1-(2,2,2-trifluoroethyl)-1H-1,2,4-triazol-5-yl]aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(ethylsulfonyl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-5-fluoro-2-(methylsulfonyl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-5-chloro-2-(methylsulfonyl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-5-methyl-2-(methylsulfonyl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-5-methoxy-2-(methylsulfonyl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-[1-isopropyl-1H-1,2,4-triazol-5-yl]aniline, and pharmaceutically acceptable salts and solvates thereof.

12. A compound of Claim 1 selected from the group consisting of  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-5-fluoro-2-(methylsulfonyl)aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(1-ethyl-1H-pyrazol-5-yl)aniline,  
 2-[(4,5-dihydro-1H-imidazol-2-ylmethyl)amino]-N-methylbenzenesulfonamide,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-[1-(2,2,2-trifluoroethyl)-1H-1,2,4-triazol-5-yl]aniline,  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(methylsulfonyl)aniline, and  
 pharmaceutically acceptable salts and solvates thereof.

13. A compound of Claim 1 selected from the group consisting of  
 N-(4,5-dihydro-1H-imidazol-2-ylmethyl)-2-(methylsulfonyl)aniline and  
 pharmaceutically acceptable salts and solvates thereof.

14. (AMENDED) A compound of [any of] Claim 1 [-13] wherein said compound is an alpha-1A agonist.

15. (AMENDED) A method for prevention or treatment of an alpha-1A mediated disease or condition comprising administration of a therapeutically effective amount of a compound of [any of] Claim [1-] 14.

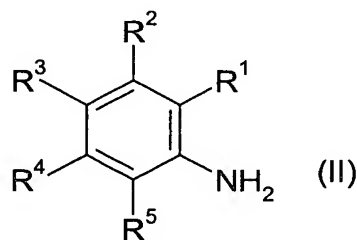
16. The method of Claim 15 wherein said disease or condition is urinary incontinence, nasal congestion, priapism, depression, anxiety, dementia, senility, Alzheimer's, deficiencies in attentiveness and cognition, and eating disorders such as obesity, bulimia, or anorexia.

17. The method of Claim 15 wherein said disease or condition is urinary incontinence.

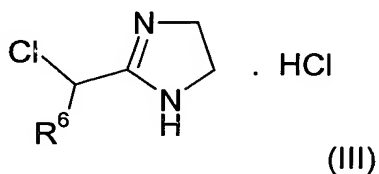
19. (AMENDED) A pharmaceutical composition comprising a therapeutically effective amount of a compound of [any of] Claim[s] 1[-14].

20. A pharmaceutical composition according to Claim 19 further comprising a pharmaceutically acceptable diluent or carrier.

24. (AMENDED) A process for preparing a compound as claimed in [any one of] Claim[s] 1 [to 14] which comprises reacting a compound of formula II:



with a compound of formula III:



25. A process as claimed in Claim 24 wherein the reaction is carried out at a pH in the range of from 3.0 to 4.0.

26. (AMENDED) A process as claimed in Claim [24 or] 25 wherein the reaction is run in a protic solvent.

27. A process as claimed in Claim 26 wherein said protic solvent is selected from the group consisting of methanol, ethanol, methoxyethanol, isopropanol, butanol, and phenol.

28. A process as claimed in Claim 27 wherein the protic solvent is 2-butanol.

29. (AMENDED) A process as claimed in [any of] Claim[s 24-] 28 wherein the reaction is run at a temperature or temperatures of from 80 to 140°C.